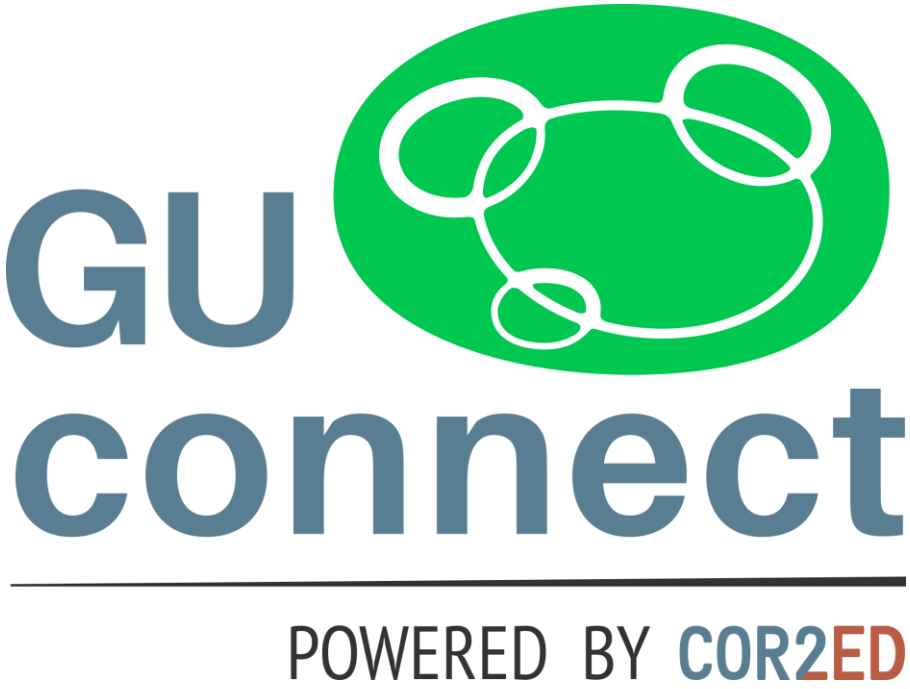
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UPDATE FROM ASCO GU
FEBRUARY 2018, SAN FRANCISCO, USA

Prof. David Pfister
University Hospital of Cologne
Germany

RENAL CELL CARCINOMA

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TREATMENT MODIFICATION WITH SUNITINIB IN 1ST LINE METASTATIC RENAL CELL CARCINOMA: AN ANALYSIS OF THE STAR-TOR REGISTRY

Boegemann M et al. Abstract #602

STAR-TOR #602

- Multicenter, prospective real world registry to report safety and outcome in patients with Sunitinib in first-line treatment of mRCC

- Patient categorisation
  1. Sunitinib initiated as standard dosage with subsequent dose modification (SM)
  2. Sunitinib as standard dosage (SS)

mRCC: metastatic renal cell carcinoma

Boegemann M et al. Abstract #602 Presented at ASCO GU 2018

STAR-TOR #602

- Outcome assessment:
  - Time on treatment
  - PFS
  - OS
  - AEs
  - International mRCC Database Consortium (IMDC) risk status

AEs: adverse events; mRCC: metastatic renal cell carcinoma; OS: overall survival; PFS: progression free survival

Boegemann M et al. Abstract #602 Presented at ASCO GU 2018

STAR-TOR #602: PATIENT CHARACTERISTICS

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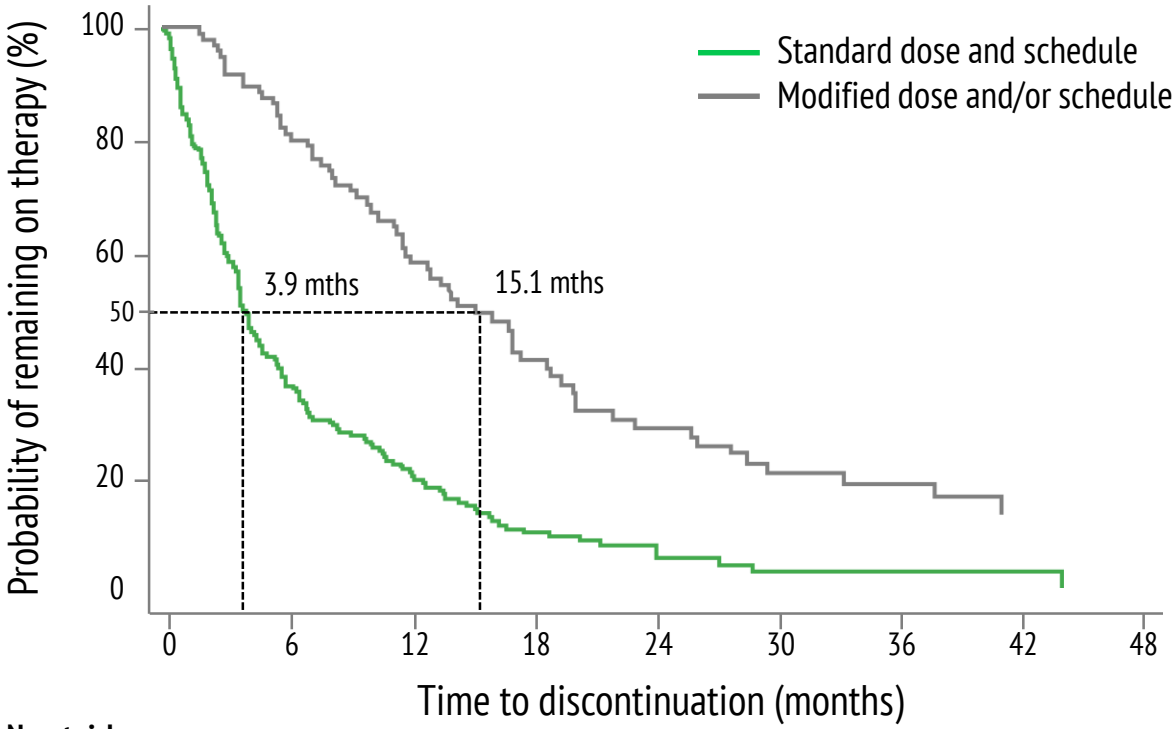
Baseline Demographics			
	Overall (n=297)	Received standard dose and schedule (n=199)	Required dose and/or schedule modification (n=98)
Age (years), median (IQR)	67.0 (59.0-74.0)	65.0 (58.0-74.0)	69.0 (62.0-74.0)[a]
Body mass index, n (%)			
Underweight (<18.5 kg/m^2)	2 (0.7)	1 (0.5)	1 (1.1)[b]
Normal (18.5-24.9 kg/m^2)	81 (28.7)	60 (32.1)	21 (22.1)
Overweight (25.0-29.9 kg/m^2)	128 (45.4)	85 (45.5)	43 (45.3)
Obese (≥30.0 kg/m^2)	71 (25.2)	41 (21.9)	30 (31.6)
Histology, n (%)			
Clear cell carcinoma	247 (84.0)	165 (83.8)	82 (84.5)
Non-clear cell carcinoma	47 (16.0)	32 (16.2)	15 (15.5)
Prior nephrectomy (full or partial), n (%)	252 (85.1)	165 (83.3)	87 (88.8)
IMDC risk status, n (%)	**n=160**	**n=107**	**n=53**
Favourable	8 (5.0)	4 (3.7)	4 (7.5)[c]
Intermediate	94 (58.8)	55 (51.4)	39 (73.6)
Poor	58 (36.3)	48 (44.9)	10 (18.9)

[a]p=0.0230; [b]p=0.0439; [c]p=0.0013

IQR: interquartile range; IMDC: international mRCC database consortium; IQR: interquartile range; kg: kilograms; m: metres

Boegemann M et al. Abstract #602 Presented at ASCO GU 2018

STAR-TOR #602: TIME ON TREATMENT



No. at risk

Standard	198*	69	31	15	5	2	2	1	0
Modified	98	76	46	29	18	11	8	4	4

Median TT (95% CI) – Standard: 3.9 (3.4-4.6) vs. Modified: 15.1 (11.7-18.7); p<0.0001

*One patient excluded with time on treatment equal to 0.

TT: time on treatment

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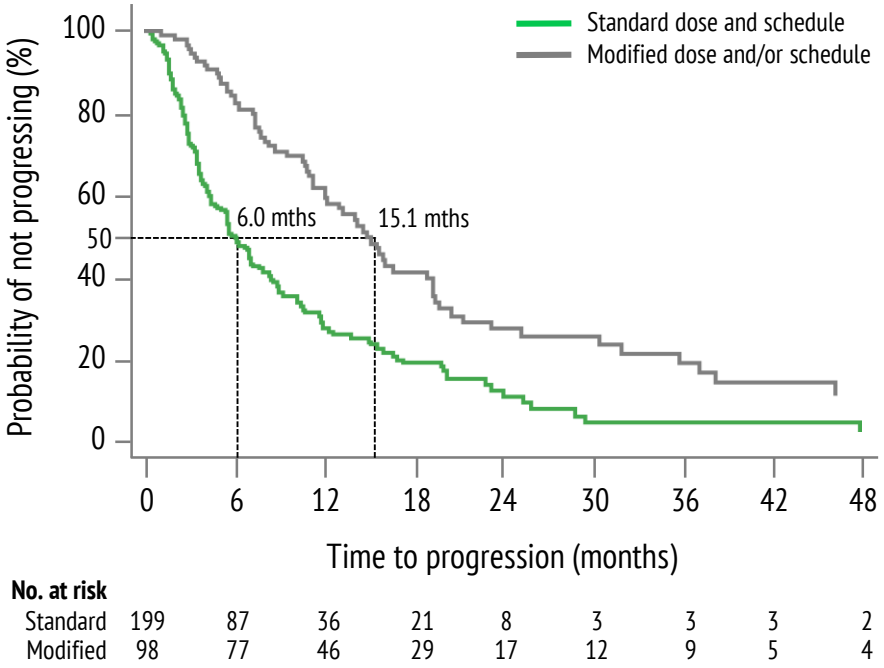
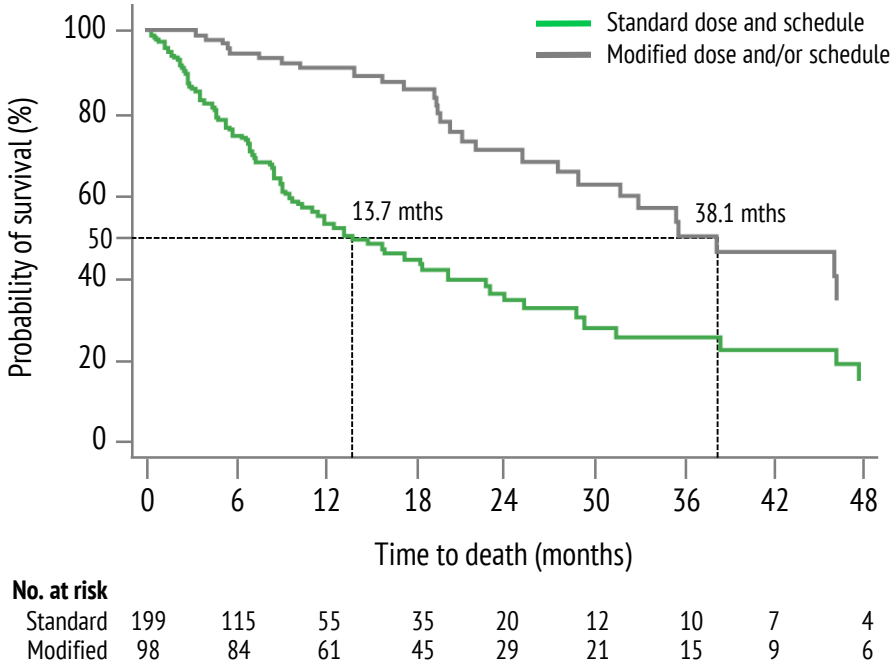
STAR-TOR #602: PFS AND OS





Median **PFS** (95% CI) – Standard 6.0 (4.7-7.6) vs. Modified 15.1 (11.9-19.2); p<0.0001

Median **OS** (95% CI) – Standard 13.7(10.1-20.2) vs. Modified 38.1 (28.9-50.5); p<0.0001

OS: overall survival; PFS: progression free survival

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STAR-TOR

- Sunitinib is a well established primary treatment in mRCC
- Patients with **dose modification** were **significantly longer on treatment**
- Longer sufficient treatment leads to a **longer PFS and OS** in the patient cohort
- Negative aspects of the trial:
  - No data are available for subsequent systemic treatment
  - There is a larger number of patients in the poor IMDC risk status in the cohort of SS (44.9%) compared to SM (18.9%)

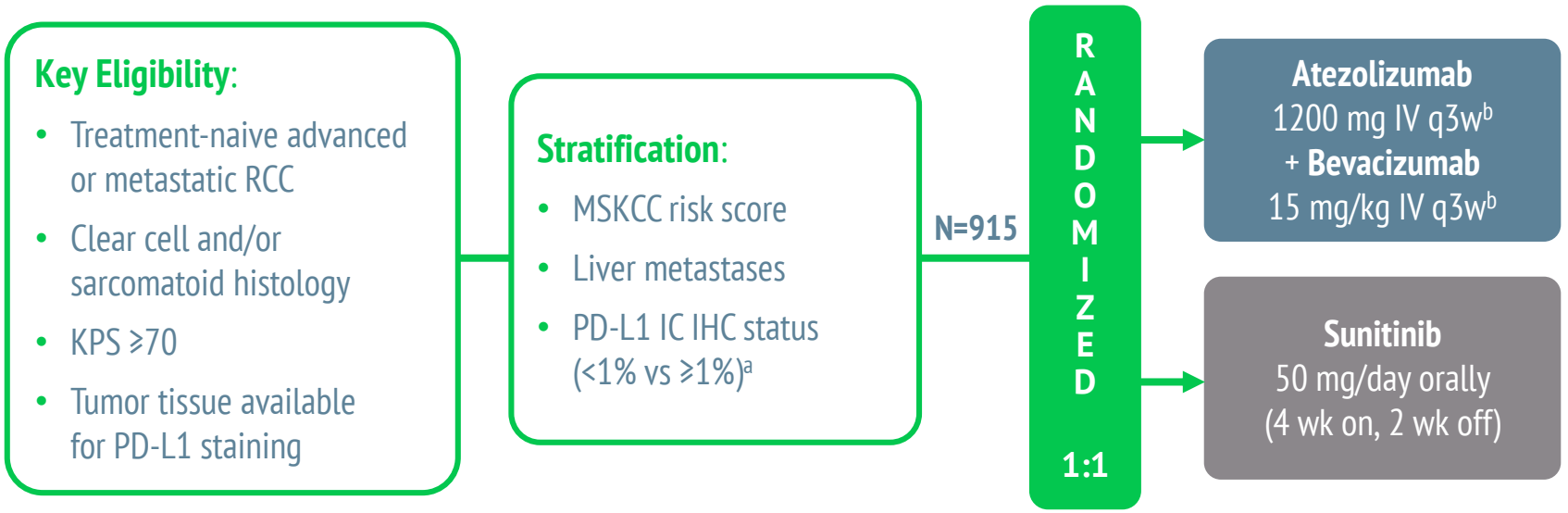
IMDC: international mRCC database consortium; mRCC: metastatic renal cell carcinoma; OS: overall survival; PFS: progression free survival; SM: subsequent dose modification; SS: standard dosage

Boegemann M et al. Abstract #602 Presented at ASCO GU 2018

IMmotion151: A RANDOMIZED PHASE III STUDY OF ATEZOLIZUMAB PLUS BEVACIZUMAB VERSUS SUNITINIB IN UNTREATED METASTATIC RENAL CELL CARCINOMA

Motzer RJ et al. Abstract #578

IMmotion151: STUDY DESIGN



[a]⩾1% IC: 40% prevalence using SP142 IHC assay;
[b]No dose reduction for atezolizumab or bevacizumab.

IC: immune cells; IHC: immunohistochemistry; KPS: karnofsky performance status; MSKCC: Memorial Sloan-Kettering Cancer Center; PD-L1: programmed death-ligand 1

Motzer RJ et al. Abstract #578 Presented at ASCO GU 2018

IMmotion151: PATIENT CHARACTERISTICS

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Characteristic	PD-L1+ (N=362)		ITT (N=915)	
	Atezo + Bev (n=178)	Sunitinib (n=184)	Atezo + Bev (n=454)	Sunitinib (n=461)
Age, median (range), y	62 (33-84)	59 (23-80)	62 (24-88)	60 (18-84)
Male, %	67%	79%	70%	76%
KPS ≥80, %	95%	95%	91%	92%
Liver metastasis, %	17%	18%	17%	18%
Prior nephrectomy, %	84%	83%	74%	72%
Predominant clear cell histology, %	92%	87%	93%	92%
Sarcomatoid component, %	20%	27%	15%	16%
≥1% of IC expressing PD-L1 (PD-L1+), %	–	–	39%	40%
MSKCC risk category, %				
Favorable (0)	17%	18%	20%	20%
Intermediate (1 or 2)	74%	73%	71%	70%
Poor (≥3)	8%	9%	10%	10%

Baseline characteristics were comparable across treatment arms and between PD-L1+ and ITT patients

IC: immune cells; ITT: intention to treat; KPS: karnofsky performance status; MSKCC: Memorial Sloan-Kettering Cancer Center; PD-L1: programmed death-ligand 1

Motzer RJ et al. Abstract #578 Presented at ASCO GU 2018

IMmotion151: PFS IN PD-L1+ PATIENTS AS PRIMARY ENDPOINT

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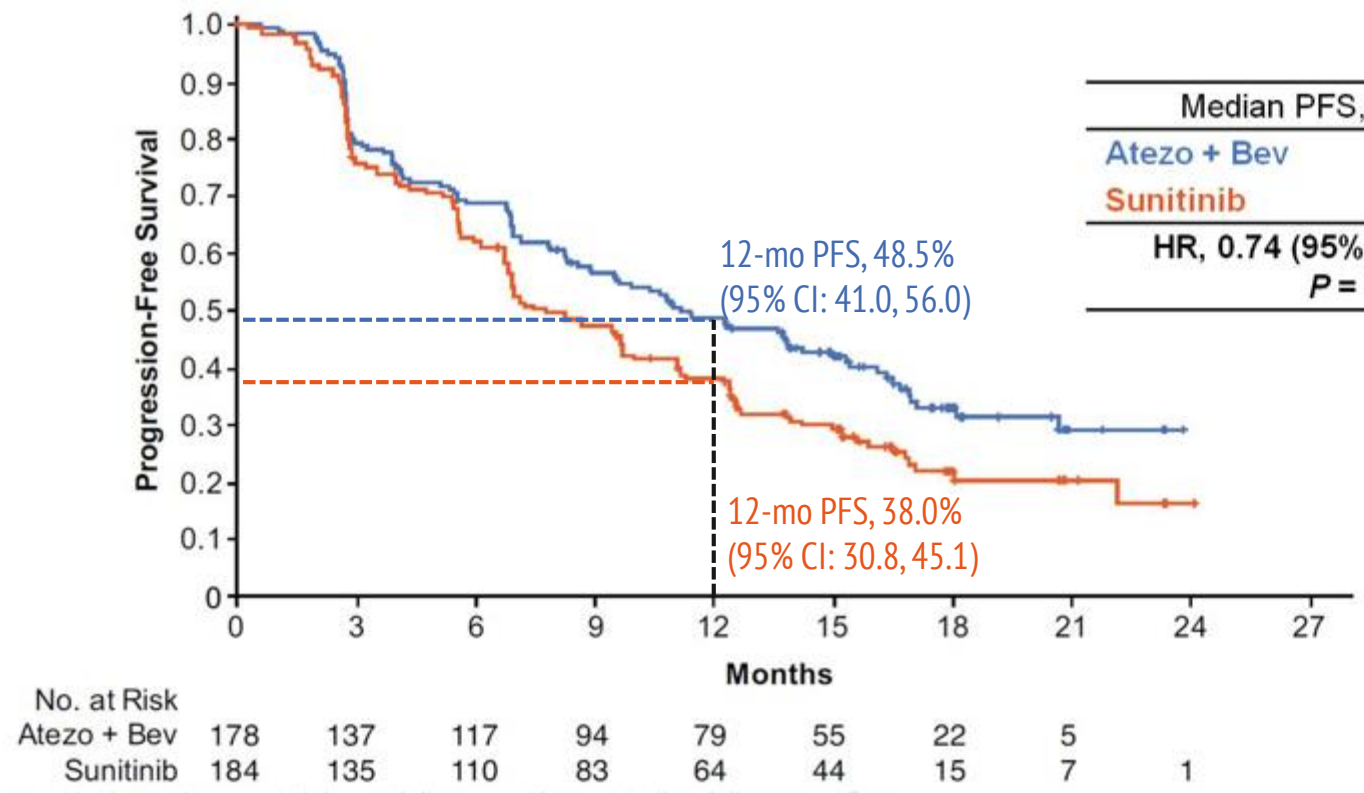

Atezo: Atezolizumab; Bev: Bevacizumab; CI: confidence interval; HR: hazard ratio; PD-L1: programmed death-ligand 1; PFS: progression free survival

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IMmotion151: PFS IN ITT PATIENTS

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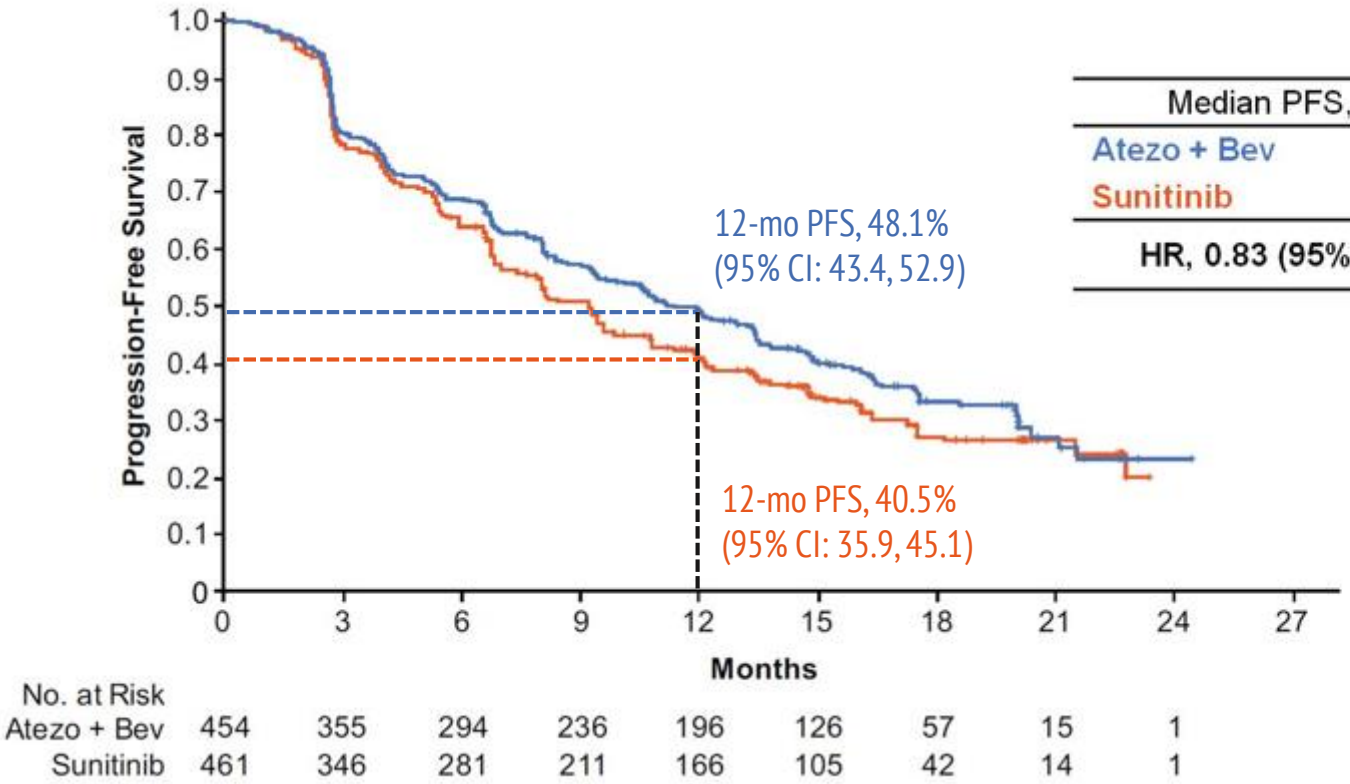
Secondary Endpoint



Median PFS, mo (95% CI)	
Atezo + Bev	11.2 (9.6, 13.3)
Sunitinib	8.4 (7.5, 9.7)
HR, 0.83 (95% CI: 0.70, 0.97)	

Atezo: Atezolizumab; Bev: Bevacizumab; CI: confidence interval; HR: hazard ratio; ITT: intention to treat; PFS: progression free survival

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IMmotion151:
OS IN ITT AS A CO-PRIMARY ENDPOINT

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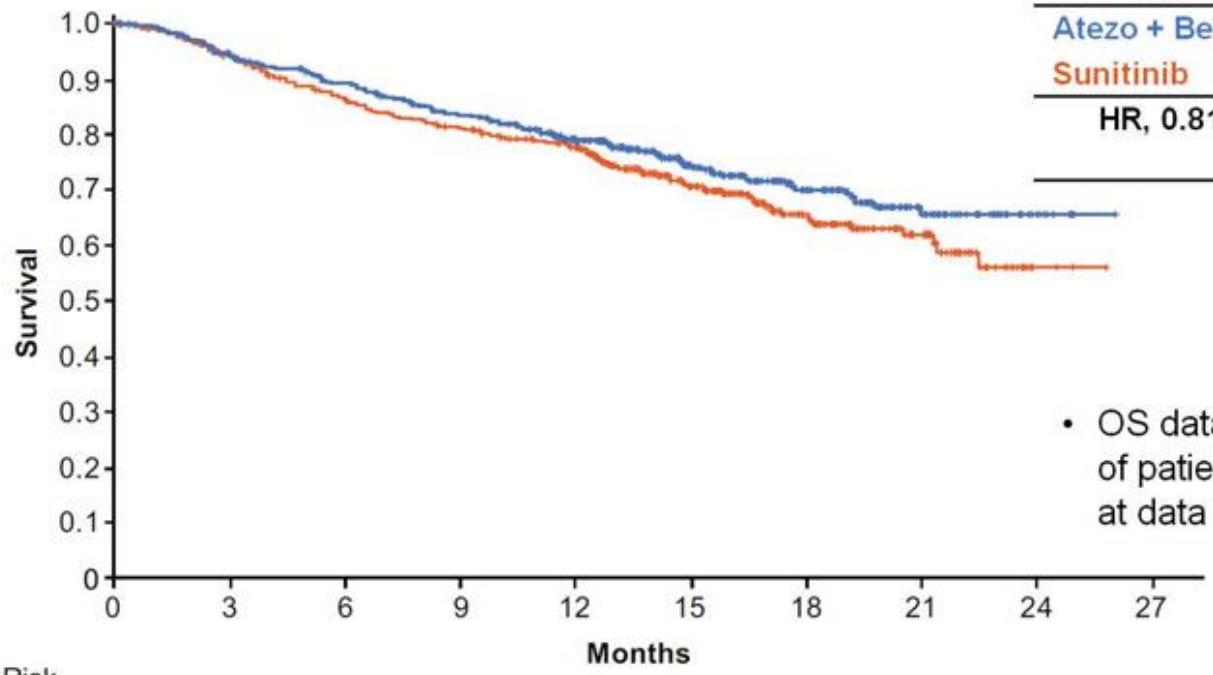
Co-Primary Endpoint

Median OS, mo (95% CI)	
Atezo + Bev	Not reached
Sunitinib	Not reached
HR, 0.81 (95% CI: 0.63, 1.03)	
P = 0.09	



- OS data are immature; 29% of patients had an OS event at data cutoff

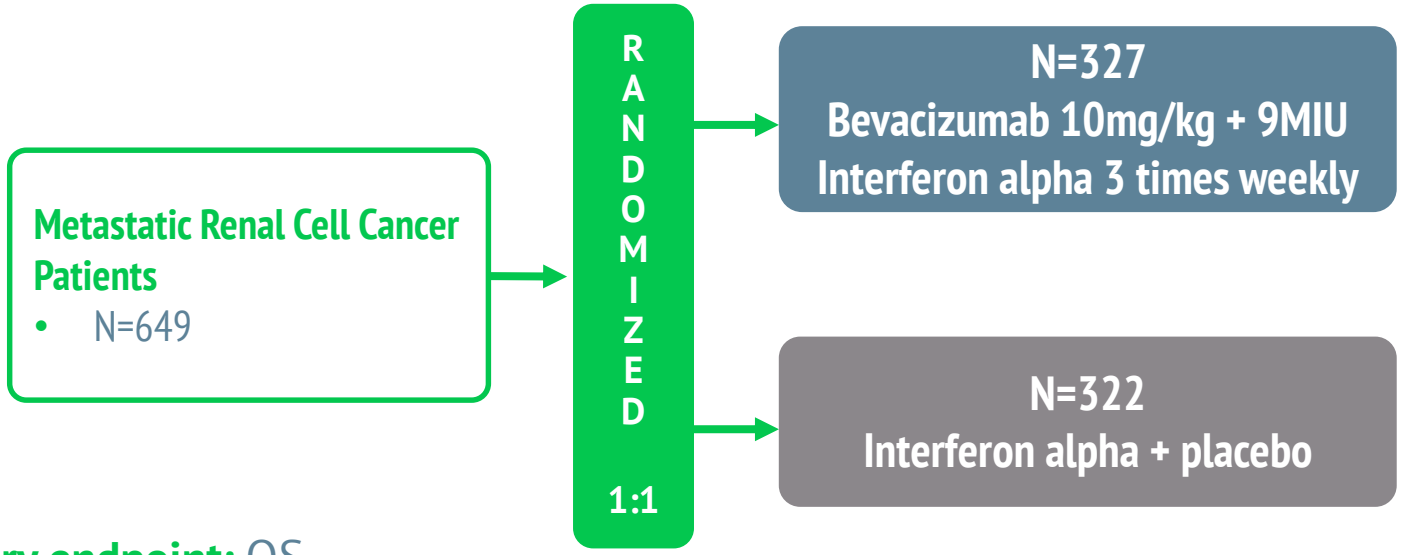
No. at Risk									
Atezo + Bev	454	428	398	371	341	246	141	69	18
Sunitinib	461	422	384	357	331	227	126	65	15

CI: confidence interval; HR: hazard ratio; ITT: intention to treat; OS: overall survival

Motzer RJ et al. Abstract #578 Presented at ASCO GU 2018

AVOREN TRIAL - BEVACIZUMAB PLUS INTERFERON ALFA-2a FOR TREATMENT OF METASTATIC RENAL CELL CARCINOMA

- Multicenter Phase III Trial prospective randomised double blind

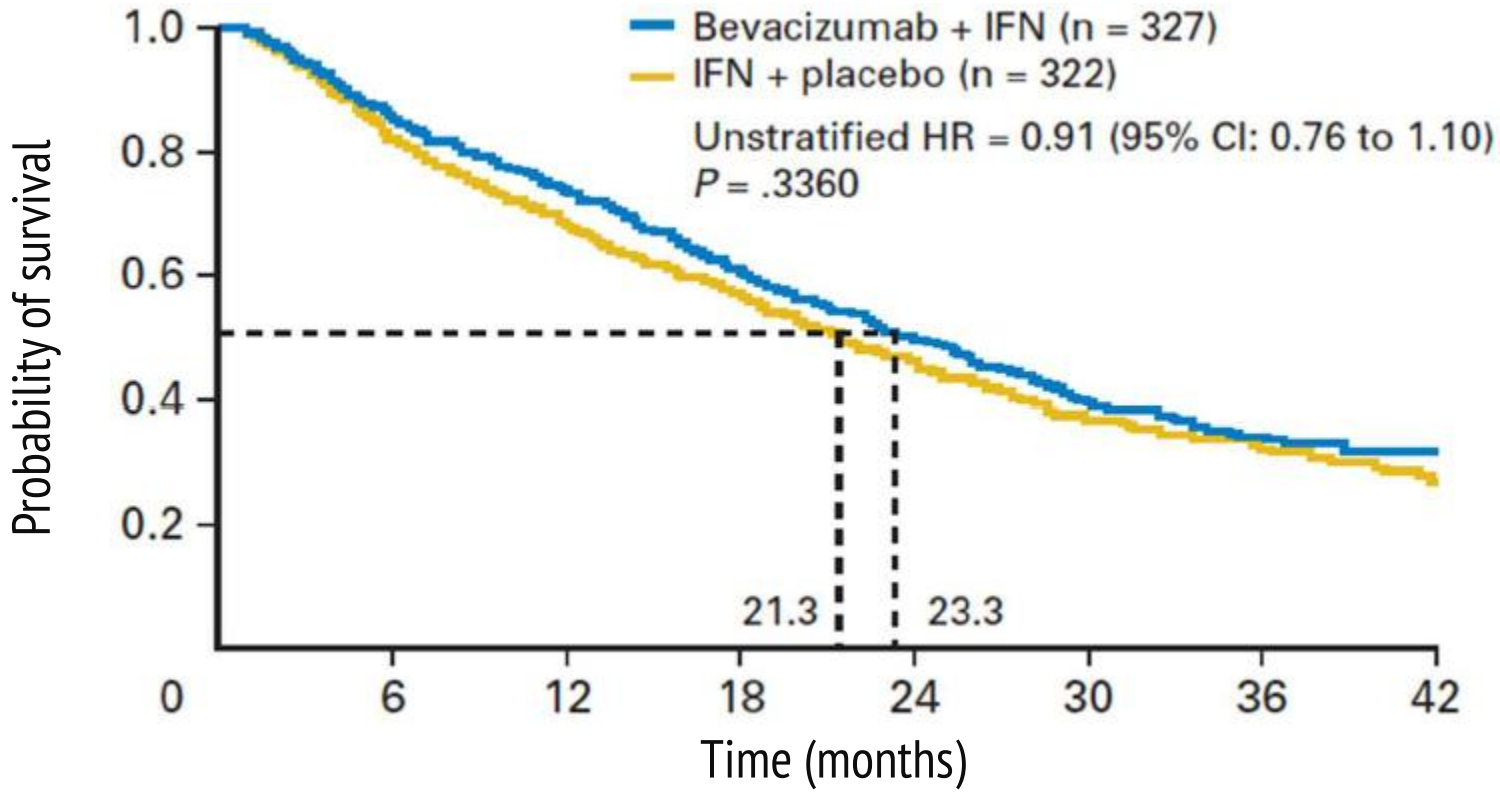


- **Primary endpoint:** OS
- **Secondary endpoint:** PFS and Safety
- PFS 10.2 versus 5.4 Months; HR 0.63, 95% CI 0.52-0.75 (p=0.0001)

CI: confidence interval; HR: hazard ratio; OS: overall survival; PFS: progression free survival

Escudier et al. Lancet oncology 2007; 370: 2103-2111

CAUTION: OS IN AVOREN TRIAL



CI: confidence interval; HR: hazard ratio; IFN: Interferon alpha; OS: overall survival

Escudier et al. J Clin Oncol 28: 2144-50

IMmotion151 TRIAL

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- Patient treated with the combination Bevacizumab and Checkpoint inhibitor Atezolizumab had a **significant longer PFS**
- Nevertheless the coprimary Endpoint OS in ITT is **not statistically significant different**
- PFS data are **comparable to the formally shown Avoren Trial**

ITT: intention to treat; OS: overall survival; PFS: progression free survival
Motzer RJ et al. Abstract #578

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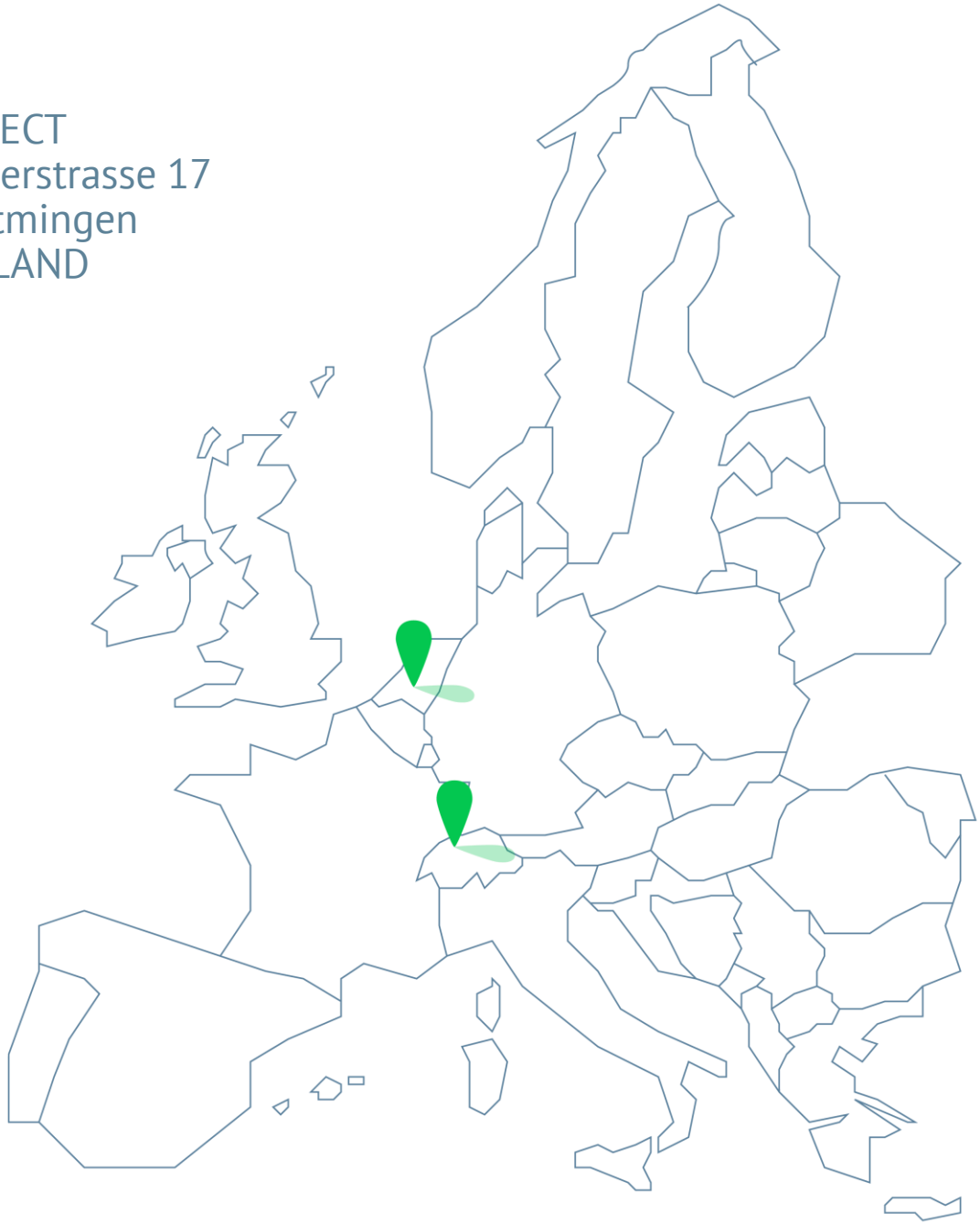

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